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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/658,986	09/10/2003	Abbot F. Clark	1581 US FA	6064

7590 10/18/2006

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EXAMINER
BASI, NIRMAL SINGH

ART UNIT	PAPER NUMBER
1646	

DATE MAILED: 10/18/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/658,986	CLARK ET AL.	
	Examiner	Art Unit	
	Nirmal S. Basi	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on *28 July 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4* is/are pending in the application.

4a) Of the above claim(s) *4* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *09 February 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *2/12/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restriction

1. Applicant's election of Group I, Claims 1-3 as they pertain to method for diagnosing glaucoma by assaying for the polynucleotide encoding GRβ, on 7/28/06, is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP 818.03(a)). Claim 4 is withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention. The requirement is still deemed proper and is therefore made FINAL.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

2. Claims 1-3 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is indefinite because it is not clear what is "aberrant expression of GRβ" so as to allow the metes and bounds of the claim to be determined. It is not clear what aberrant expression of GRβ in a patient indicates a diagnosis of glaucoma.

Claim 2 is indefinite because it is not clear what "defect in the GRβ isolated from said sample" alters the degree of alternating splicing so as to allow the metes and bounds of the claim to be determined. Further it is not clear "what degree of alternating splicing between exons 8 and 9α/9β" lead to altered expression of GRβ and indicate a diagnosis of glaucoma. Also it is not clear to which protein exons 8 and 9α/9β belong and what amino acid sequence identifies said exons so as to allow the metes and bounds of the claim to be determined

Claim 3 is indefinite because it is not clear what is the "defect in the GRβ isolated from said sample" that alters the degree of alternating splicing so as to allow the metes and bounds of the claim to be determined. Further it is not clear how the defect is specifically detected by using the claimed assays so as to allow the metes and bounds of the claim to be determined. Claim 3 is also rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: those required to identify the "defect in the GRβ isolated from said sample". The mere mentioning general assays does not disclose the specific conditions, probes etc required to detect the defect or even identify the defect. Further is not clear what are the assay steps in the restriction fragment length polymorphism (RFLP), single-stranded conformation polymorphism (SSCP), polymarase chain reaction (PCR), denaturing gradient gel electrophoresis; allele specific oligonucleotide ligation, and allele specific hybridization as they specifically relate to identifying the "defect in the GRβ

isolated from said sample" and indicating a diagnosis of glaucoma. The specification only mentions said assays on pages 4 and 5 without further clarification as to what the assays encompass as they specifically relate to determing the defect in instant invention. Clarification is needed as to allow the metes and bounds of the claim to be determined.

Claim 3 rejected due to the improper Markush grouping. The claim refers to a group containing both methods and non-methods. Single-stranded conformation polymorphism (SSCP) is not a method.

Claim 2 is objected to because it is not clear what is meant by "expressio" on line 4 of subsection (c). This appears to be typographical error. If this is indeed the case the objection can be overcome by amending the claim to read "expression".

Claim Rejection, 35 U.S.C. 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. Claims 1-3 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for diagnosing glaucoma in a patient wherein a decrease in GRβ (SEQ ID NO:1) expression in the trabecular meshwork of a patient as compared to the expression of GRβ (SEQ ID NO:1) in the trabecular meshwork of a non-glaucomatous patient indicates a diagnosis of glaucoma, does not reasonably provide enablement for other methods for diagnosing glaucoma in a patient. The specification does not enable any person

skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

Claims are drawn to a method of diagnosing glaucoma which comprises detecting aberrant expression of the GRβ or defects in a GRβ . The claims suggest possible general assays which may be used to achieve the goal of the preamble but the specification, claims or prior art do not state how to use said assays to specifically diagnose glaucoma and no indication of the arrangement of the method steps is given. The specification discloses a method for diagnosing glaucoma in a patient wherein a decrease in GRβ (SEQ ID NO:1) expression in the trabecular meshwork of a patient as compared to the expression of GRβ (SEQ ID NO:1) in the trabecular meshwork of a non-glaucomatous patient indicates a diagnosis of glaucoma. Therefore a direct comparison of the GRβ nucleic acid of SEQ ID NO:1 in the trabecular meshwork of normal patients as compared to that found in the trabecular meshwork of non-glaucomatous patient is the only example of "aberrant expression" or "defect" disclosed in the specification that allows the diagnosis of glaucoma in a patient. Although other patterns of aberrant expression or defects may exist they may indicate glaucoma in a patient none of these are identified in the specification, apart from the one disclosed as enabling above.

Prior art and the specification disclose that various tissues express the both GRα and GRβ, and that the alternate splice form, GRβ , does not bind

glucocorticoids. The specification states that" Surprisingly, it has been found that cultured human trabecular meshwork cell lines express the proteins for both an alternate splice form of the human glucocorticoid receptor (GRβ; SEQ ID NO:1), as well as the normal glucocorticoid receptor (GRα; SEQ ID NO:3). The specification discloses that elevated intraocular pressure associated with primary open-angle glaucoma may be due to the aberrant expression of GRβ in the tubular meshwork. The specification concludes that determining that an individual abnormally expresses GRβ in their trabecular meshwork tissue can lead to a diagnosis of glaucoma.

Therefore, the lack of guidance provided in the specification as to what other aberrant expression of GRβ SEQ ID NO:1, except for that as disclosed enabling for claimed invention, would prevent the skilled artisan from determining whether any other modification or mutation to the GRβ could be detected that would indicate glaucoma in a patient without undue experimentation. Due to the large quantity of experimentation necessary to identify other defects in the GRβ and the lack of direction/guidance presented in the specification regarding the identification, purification, isolation and characterization of said defects, the unpredictability of the effects of mutation on the structure and function of proteins, and the breadth of the claim which encompass undefined defects and aberrant expressions, undue experimentation would be required of the skilled artisan to make or use the claimed invention in its full scope.

4. No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nirmal S. Basi whose telephone number is 571-272-0868. The examiner can normally be reached on 9:00 AM-5:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Nickol can be reached on 571-272-0835. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Nirmal S. Basi
Art Unit 1646
October 16, 2006

EILEEN B. O'HARA
PRIMARY EXAMINER